Figures 4A-C illustrate the percent change in DXA measures of the spine for control and treatment groups in the lumbar vertebrae 2-4 for bone area (A), bone mineral content (B), and bone mineral density (C).

Figures 5A and 5B illustrate the increase in bone mass (A) and bone strength (B) in lumbar vertebrae of primates treated with a parathyroid hormone.

Figures 6A and 6B illustrate the increase in strength of femur neck (A) and the constant strength of humerus mid-diaphysis (B) in primates treated with a parathyroid hormone.

Figure 7 illustrates activation of bone formation rates on endosteal and periosteal surfaces of the midshaft humerus.

Figure 8 illustrates the histogram analysis of the shift in bone voxel densities in lumbar vertebra, resulting from PTH treatment compared to control. Note the increase in density in cortical bone compartment after withdrawal of PTH treatment.

Figure 9 illustrates increases in lumbar spine BMD through 23 months of treatment of patients with either 20 μg/kg/day PTH or 40 μg/kg/day PTH, compared to placebo treated controls.

Figure 10 illustrates increases in femur and hip neck BMD through 24 months of treatment of patients with either 20 μg/kg/day PTH or 40 μg/kg/day PTH, compared to placebo treated controls.

DETAILED DESCRIPTION

The invention relates to a method for increasing bone toughness and/or stiffness, and/or reducing incidence of fracture in a subject by administering a parathyroid hormone. The method can be employed to increase stiffness and/or toughness at a site of a potential trauma or at a site of an actual trauma. Trauma generally includes fracture, surgical trauma, joint replacement, orthopedic procedures, and the like. Increasing bone toughness and/or stiffness generally includes increasing mineral density of cortical bone, increasing strength of bone, increasing resistance to loading, and the like. Reducing incidence of fracture generally includes reducing the likelihood or actual incidence of fracture for a subject compared to an untreated control population.

Patient Characteristics

	Placebo (N=544)	PTH-20 (N=541)	PTH-40 (N=552)	p-value
Caucasian	98.9%	98.9%	98.4%	0.672
Age	69.0±7.0	69.5±7.1	69.9±6.8	0.099
Years post menopausal	20.9±8.5	21.5±8.7	21.8±8.2	0.273
Hysterectomized	23.8%	23.1%	21.6%	0.682
Uterus + 0 or 1 ovary	57	51	58	
Uterus + 2 ovaries	61	57	51	
Unknown	11	17	10	
Previous osteoporosis drug use	14.9%	15.5%	13.0%	0.479
Baseline spine BMD	0.82±0.17	0.82±0.17	0.82±0.17	>0.990
Baseline # of vert. fx				>0.990
0	54 (10.4%)	45 (8.8%)	54 (10.1%)	
1	144 (27.8%)	159 (31.1%)	169 (31.6%)	
2	128 (24.7%)	128 (25.0%)	125 (23.4%)	
3	75 (14.5%)	67 (13.1%)	81 (15.1%)	
4	59 (11.4%)	49 (9.6%)	45 (8.4%)	
5	28 (5.4%)	31 (6.1%)	21 (3.9%)	
6	13 (2.5%)	20 (3.9%)	25 (4.7%)	
7	6 (1.2%)	7 (1.4%)	10 (1.9%)	
8	9 (1.7%)	5 (1.0%)	3 (0.6%)	
9	1 (0.2%)	0	2 (0.4%)	
10	1 (0.2%)	1 (0.2%)	0	
Unspecified	26	29	17	

Results

Data from this clinical trial including a total of 1637 women treated with recombinant human parathyroid hormone (1-34), rhPTH(1-34) 0, 20, or 40 μg/kg/day, and supplemented with vitamin D and calcium, for 18-24 months, showed results reported in Tables 15-19.

Table 15 illustrates data showing the reduction upon treatment with PTH of the number and severity of vertebral fractures. Comparing all PTH treated patients with placebo, the overall reduction in number of patients with vertebral fractures was 67% ($p<0.001$), with a 65% reduction ($p<0.001$) at 20 μg/day PTH compared to placebo, and a 69% reduction at 40 μg/day PTH compared to placebo (Table 15). Comparing all PTH treated patients with placebo, the overall reduction in number of patients with multiple vertebral fractures was 81% ($p<0.001$), with a 77% reduction